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(Translated by Ostertag)

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## TOXICOLOGICAL EVALUATION OF AMMONIUM SULFAMATE - A HERBICIDE PREPARATION

Following is a translation of an article by M. K. Vinokurova and V. B. Mal'kova (Saratov), Institute of Rural Hygiene, published in the Russian-language periodical *Gigiyena Truda i Professional'nyye Zabolevaniya* (Industrial Hygiene and Occupational Illnesses) 7(5) 1963 pp 56-57. Translation performed by Sp/6 Charles T. Ostertag Jr.

Sulfamic acidic ammonium (ammonium sulfamate)  $\text{NH}_2-\overset{\overset{\text{O}}{\parallel}}{\underset{\underset{\text{O}}{\parallel}}{\text{S}}}-\text{O}-\text{NH}_4$

is related to the derivatives of sulfamic acid. It is a crystalline substance of a white or yellowish color with a boiling point of 125°, hygroscopic and well soluble in water. Ammonium sulfamate is a herbicide with a contact and penetrating effect. It is used in the form of a solution for spraying plants and in a dry form for application into the soil (Al'gren and others, Yu. A. Baskakov).

Published data concerning the toxic properties of ammonium sulfamate is very brief. Thus, according to information presented by Al'gren et al., feeding it to sheep in doses of 125 g didn't cause the illness of these animals. Ambrose's laboratory investigations on white rats showed that with an intraabdominal administration of the preparation in a dosage of 1.6 g to 1 kg of body weight it caused the death of some of the experimental animals. The same dose when administered into the stomach didn't cause the death of the animals. The continuous oral influence of sulfamate in the form of a 2% admixture to the rats' ration led to a considerable lowering of their gains in weight.

We investigated a commercial preparation of ammonium sulfamate (locally produced) appropriate for industrial conditions. The preparation has the appearance of dingy white crystals which are well soluble in water.

With a single administration of ammonium sulfamate in the stomach in the form of an aqueous solution of 0.5 ml for mice and 1 ml for rats, the parameters of toxicity were established from the maximum endurable up to the absolute lethal dose. The data obtained from these experiments, integrated according to Berens, show that the LD<sub>50</sub> for mice equals 3.1 g/kg and for rats 4.4 g/kg. The LD<sub>100</sub> is correspondingly 4.75 and 5.5 g/kg. In 5-10 minutes following the administration of the toxic chemicals, the animals laid down on their sides and their respiration became interrupted.

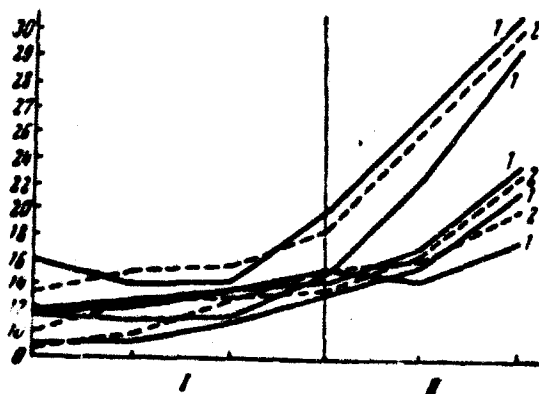
The mice died in terms ranging from 30-40 minutes up to 3-4 hours and in rare cases 24 hours. Before death, both in the mice and in the rats there were intermittent cramps. During this the rats often emitted squeaks. In more remote periods there were no deaths of animals.

Upon investigating the blood of rats which survived in acute experiments, we noticed, two days after poisoning, a lowering in the amount of leucocytes in comparison with the initial amount ( $P < 0.05$ ). Based on other indices, statistically reliable changes were not detected. Subsequently, during observation over a period of a month and longer, no signs of intoxication were noted in the experimental mice and rats.

With the administration into the stomach of 1/10 and 1/5 of the  $LD_{100}$  of ammonium sulfamate daily for a period of 25-30 days, the animals (mice and rats) summarily received 3 - 4.5 of an absolutely lethal single dose. There were no animal deaths during this. In the period of administration of the toxic chemical we noticed an increased aggressiveness of the rats in comparison with the controls which were simultaneously administered water. By external features they were no different from healthy animals. During the course of the experiment completely healthy progeny of mice were born and grew. Upon morphological investigation of the internal organs of rats slaughtered after the experiment, existing differences weren't detected in comparison with control animals. Thus the results obtained by us in the experiments with oral administration showed that ammonium sulfamate is a substance comparatively mildly toxic and under conditions of conducting experiments it didn't possess cumulative properties.

The influence of ammonium sulfamate on the skin and the possibility of a resorptive effect during this we investigated on mice by submerging their tails in a solution of the toxic chemical and on rabbits by the generally accepted method. These and other experiments were conducted using a 20% solution of the preparation. During application over a period of 20 days at two hours a day there periodically appeared on the skin of the mice' tails abrasions which gradually healed. In their general condition and dynamics of weight these animals were no different from the control. As is shown in the sketch, the fluctuations in weight of the experimental and control mice were completely analogous.

In experiments on rabbits, which continued for 30 days, a local affection of the skin and a general toxic effect of applications of sulfamate also weren't apparent. According to the blood picture and the phagocytic activity of the leukocytes and the relationship of the protein fractions of blood serum, the experimental rabbits were essentially no different from the control. Application of a drop of a 20% solution of the preparation on the mucous membrane of the rabbit's eye didn't show a noticeable effect.



[Chart from page 57 of the original.] Dynamics of weight of mice under the action of ammonium sulfamate on the skin (tail). Angle of abscissa -- weight (in grams); angle of ordinate -- time (in days); 1 -- experimental, 2 -- control.

We investigated the effect of ammonium sulfamate through the respiratory routes on rats by means of inoculating them in a chamber into which a 20% solution of the herbicide in the form of an aerosol is admitted. The inoculations were conducted over a period of a month. During this the daily concentrations of ammonium sulfamate in the chamber were within the limits of 0.25 - 0.5 mg/l. In the first period of inoculations (1-2 weeks) we observed, during the exposure of the rats, discharges from the nose and sometimes sneezing; upon continuation of the inoculation the irritating effect of the aerosol of ammonium sulfamate was detected less often. In the experimental animals the weight increase lowered in comparison with the control animals and based on other indicators there were noted some changes of the protein fractions of the blood due to an increase ( $P < 0.05$ ) of gamma-globulins. Upon continuation of the inoculations these indicators were reduced and externally the experimental rats weren't noticeably different from the control.

It was established by morphological investigations that in some of the experimental animals which were slaughtered, upon conclusion of the inoculations there was scaling of the epithelium of the mucous membrane of the trachea and the large bronchi.

The experiments showed that under specific conditions an aerosol of ammonium sulfamate may irritate the mucous membranes of the respiratory tract. To this it must be added that when setting up several experiments with an aerosol of the preparation the laboratory workers perceived a tickling or itching in the throat and a tingling in the nose (during this the concentrations of sulfamate in the zone of respiration was established within the limits of 0.1 - 0.2 mg/l). This effect was easily eliminated by use of a common gauze bandage.

## CONCLUSIONS

1. Ammonium sulfamate is a comparatively weakly toxic substance. With oral administration the LD<sub>50</sub> for mice equals 3.1g to 1 kg of body weight, for rats - 4.4g/kg.
2. There were no accumulative properties of ammonium sulfamate detected.
3. The effects of numerous exposures to an aerosol of ammonium sulfamate in concentrations of 0.25 - 0.5 g/l caused the occurrence of desquamated catarrh of the upper respiratory tract.
4. The application of a 20% solution of ammonium sulfamate on the skin may cause an infraction of the entirety of the surface layer of skin; there is no overall toxic influence detected during this.
5. From a hygienic point of view ammonium sulfamate may be widely used in agriculture with the application of the usual measures of protecting the respiratory organs and exposed parts of the skin.

Footnote <sup>1</sup> Morphological examination performed by S. A. Stepaov.

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